REMARKS

Reconsideration of the examiner's outstanding rejections is respectfully requested.

Sincere appreciation is expressed to the examiner for the helpful interview of December 16, 2008. It is believed that this response and the attachments alleviate the examiner's concerns about the efficacy of the prior declaration under 37 C.F.R. 1.132.

Being filed herewith is evidence that L19 has been deposited with the ATCC during prosecution of co-pending application 10/321,558. This deposit renders moot the examiner's rejection under 35 U.S.C. 112.

However, for the record, it is noted that L19 is properly described as an "scFv" or as an "antibody" or as a "scFv antibody." These terms are used interchangeably in the field with no confusion whatsoever. In this regard, note the cited Viti et al. (1999) reference, under "MATERIALS AND METHODS." The first paragraph states: "The isolation of the E1 and L19 Abs has been described previously (18). E1 is a scFv binding to the ED-B domain of fibronectin that is isolated from a synthetic human phage display Ab library Ab library. L19, a mutant of E1 with 760-fold improved affinity, differs from the parental Ab by eight mutations . . .The genes coding for scFv (E1) and scFv (L19) . . . The corresponding Ab fragments . . ." Clearly, the terms at issue are used interchangeably. In the art, scFv's are referred to as antibodies. In any event, in accordance with the interview, this issue is being rendered moot by the establishment of the deposit of L19.

As discussed during the interview, the examiner's analysis of the previously submitted Licha declaration recognizes its "showing of increased fluorescence" and of "increased immunoreactivity." Office Action of November 30, 2007. The examiner provides three reasons to support her allegation that the showing does not establish unexpected results. As discussed during the interview, these reasons do not support such contention.

Firstly, the second Licha declaration being filed herewith, establishes that the antibody in all five conjugates was effectively the same. (Previously, it was stated by the undersigned, based on information and belief, that the antibody was precisely the same in all five conjugates. However, upon further investigation by in-house counsel of the assignee corporation, it has been determined that this statement was inadvertently imprecise, as explained herein. Any inconvenience is regretted.)

The antibody L19 itself is A in conjugates 1 and 5 of the Declaration. In conjugates 2-4 of the declaration, the conjugated moiety is not L19 per se, but rather L19-cisTag. The latter moiety is known as AP39. As stated by the declarant, the presence of the cisTag moiety on L19 has no measurable effect on the immunoreactivity or fluorescent quantum yield obtained in the conjugates 2-4.

In view of this clarification, the examiner's first reason is now rendered moot,

The examiner's third reason was the result of an inadvertent error, as the undersigned understands the content of the interview. The examiner states that the showing of increased immunoreactivity for the antibodies of conjugates 1-4 over that of the antibody in conjugate 5 would be expected, for reasons alleged with respect to Viti et al. However, since the antibodies in all five conjugates are effectively the same, the prior art cannot possibly lead a skilled worked to expect immunoreactivity differences.

The remaining reason (Number 2 on page 8 of the Office Action of November 30, 2007) alleges that the established increased fluorescence shown in the Table on page 4 of the first Licha declaration is not unexpected because Licha states that the cyanine dyes in such reference "have one thousand times greater fluorescence intensity" and "have little protein affinity." Allegedly, this would lead one of ordinary skill in the art to "expect to see an increased signal." However, Licha et al. does not state that its dyes have increased fluorescent intensity or less protein affinity with respect to the closest prior art dye used in the Neri et al. reference. The Licha et al. prior art reference at issue does not elucidate the basis for its statement. Thus, the disclosure does not lead to an expectation that the dye used in conjugates 1-4 of the invention would have a greater fluorescence quantum yield than any particular other dyes, including that used by the Neri et al. reference (conjugate 5).

Consequently, there is no basis of record which would lead a skilled worker to expect the superior properties (fluorescence quantum yield and immunoreactivity) established in the declaration of record for the invention.

Applicants wish to clarify certain other aspects of the declaration. It will be noted that conjugates 2 and 4 of the Licha declaration contain a succinimide group in the linker portion. Whereas this particular structural moiety does not fall literally within the scope of such portion in the claims of this application, these conjugates have been included as related compounds sharing sulphoalkyl substituents which are lacking in the prior art conjugate of Neri et al.

With respect to the latter conjugate, the prior art Neri et al. article states that its dye is "CY7." Such dye does not have the same structure as that used in conjugate 5 of the Licha declaration. Rather, the structure employed in conjugate 5 is even closer to the invention than is the closest prior art Neri et al. dye. The latter contains as a substituent on the –N= atom which does not bear the A antibody group, instead of the declaration's carboxypentyl moiety, rather an ethyl moiety. In the corresponding position of conjugates 1-5, this invention bears sulphobutyl or sulphoethyl moieties. Clearly, carboxypentyl is much closer to such structures than is ethyl. When comparing the closest prior art, it is probative of patentability to compare a compound which is even closer to the invention. *In re Grasselli*, 713 F2d 731 (Fed. Cir. 1983).

It will also be noted that all the compounds of the declaration are shown as salts. It is, of course, self evident to a person of skill in the art that these compounds when in admixture with a conventional buffer will produce an equilibrium between the weak acid/conjugate base or weak base/conjugate acid.

In view of the foregoing, it can be seen that all rejections should be withdrawn.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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